FOOD AND DRUG ADMINISTRATION

Memorandum

DATE: June 6, 2007

FROM: Joshua C. Nipper, Biomedical Engineer
Gastroenterology and Renal Devices Branch/DRARD, HFZ-470

SUBJECT: K070320/S1 – Traditional 510(k)
Edwards Aquarius System
Edwards Lifesciences Services, Gmbh

Robert Madjno
Director of Regulatory and Quality Affairs
Edwards Lifesciences Services, Gmbh
Edisonstrasse 6
85716 Unterschleissheim
Germany
Phone: +49 89 95475 203
Fax: +49 89 95475 301
Email: robert_madjno@edwards.com

BACKGROUND

This is my second review of this traditional 510(k) submission. The first review resulted in the file being placed on telephone hold (via email) on April 17, 2007. This submission attempts to address the deficiencies that were identified in that email. The proposed device is the Aquarius System, manufactured by Edwards Lifesciences Services, Gmbh ("Edwards" or "the firm"). The proposed device is regulated under **21 CFR §876.5860**, high permeability hemodialysis delivery system, and is a Class **II** device. The product code for this device is **78-KDI**. The general requirements for these devices are outlined in the FDA guidance document "Guidance for Industry and CDRH Reviewers on the Content of Premarket Notifications for Hemodialysis Delivery Systems; Final". The firm has stated that the proposed device is built on the same framework (hardware and software) and the Baxter Accura System (K021615), which they are using as their primary predicate device.

INDICATIONS FOR USE

As stated by the firm, "The Edwards Aquarius System in indicated for continuous solute and/or fluid removal in patients with acute renal failure of fluid overload. The Edwards Aquarius system may also be used in Therapeutic Plasma Exchange (TPE) therapies. The Edwards Aquarius system is indicated for use in a clinical setting and not for home use." With the exception of the addition of the last sentence, this indication for use is identical to the Baxter Accura System.

DEVICE DESCRIPTION

The Aquarius system is considered a hemodialysis delivery system intended for continuous renal replacement therapy (CRRT). The Aquarius is capable of delivering the following types of CRRT:

- Slow Continuous Ultrafiltration (SCUF): Provides fluid removal via ultrafiltration. A fluid flow diagram for SCUF therapy has been provided on page 11.13 of the original submission.
- Continuous Veno-venous Hemofiltration (CVVH): Provides convective solute clearance by hemofiltration. Net fluid removal (ultrafiltration) can also be prescribed during CVVH. CVVH can be performed using either pre-dilution (e.g., infusion of fluid before the blood pump), post-dilution (e.g., infusion of fluid after the blood pump), or a combination of the two. A fluid flow diagram for CVVH therapy has been provided on page 11.14 of the original submission.
- Continuous Veno-venous Hemodialysis (CVVHD): Provides diffusive solute clearance by hemodialysis. Net fluid removal (ultrafiltration) can also be prescribed during CVVHD. A fluid flow diagram for CVVHD therapy has been provided on page 11.15 of the original submission.
- Continuous Veno-venous Hemodiafiltration (CVVHDF): Provides solute clearance by both convection and diffusion. Net fluid removal (ultrafiltration) can also be prescribed during CVVHDF. Fluid infusion during CVVHDF can only be performed using post-dilution. A fluid flow diagram for SCUF therapy has been provided on page 11.16 of the original submission.
- Therapeutic Plasma Exchange (TPE): Provides plasma exchange through membrane based filtration. A fluid flow diagram for TPE therapy has been provided on page 11.17 of the original submission.

The Aquarius system is a hemodialysis delivery system developed by MeSys in Germany, and is virtually identical to the Baxter Accura System (K021615). The Aquarius is built on the same hardware framework as the Accura, with relatively minor changes (discussed in the comparison section below). The firm has stated that the software of the Aquarius has been updated since the clearance of the Accura. In order to perform the treatment, the Aquarius leads the caregiver through 9 treatment modes: System Test → Preparation → Priming → Clamp and Pressure Test → Recirculation → Connect Patient → Treatment → Disconnect Patient → End Treatment. In order to achieve these functions, the Aquarius utilizes the following component:

- Blood Pump – The blood pump can be set from 30 mL/min to 450 mL/min, or from 10 mL/min to 200 mL/min when the Aquarius is operating in "low flow" mode. The blood pump is responsible for pumping the blood from the patient's access, through the filter, and back to the patient. It should be noted that the Aquarius system can only operate in "double needle" mode.
- Filtration Pump – The filtration pump is responsible for pumping any effluent and/or used dialysate from the filter and into the filtration collection bag.
- Pre-dilution substitution pump – The pre-dilution pump is responsible for pumping substitution fluid from the bag on the scale into the blood tubing line prior to the blood pump. The pre-dilution pump does not run during SCUF or TPE, may or may not be used

during CVVH, and is used as a dialysate pump during CVVHD and CVVHDF. For CVVH, the pre-dilution and post-dilution pump rate cannot exceed 10 L/hour.

- Post-dilution substitution pump – The post-dilution pump is responsible for pumping substitution fluid from the bag on the scale into the blood tubing line after the blood pump. The post-dilution pump does not run during SCUF or CVVHD, may or may not be used during CVVH, and is used for solution infusion during CVVHDF and TPE.
- Pressure Sensors – The Aquarius system has a pressure pod on the blood tubing line before the blood pump (Access Pressure), after the blood pump but before the filter (Pre-Filter Pressure), and immediately following the filter (Return Pressure). An additional pressure sensor is located on the filtrate line, following the blood leak detector. Transmembrane pressure (TMP) is calculated using the equation: TMP = ((Return pressure + Pre-Filter Pressure)/2 – Filtrate Pressure).
- Anticoagulant Pump – The anticoagulant pump is a dc linear pump, designed to pump heparin into the blood line, after the blood pump, at a programmed rate ranging from 0 to 15 mL/hour. A heparin bolus of 0 to 2.5 ml/hour can also be programmed.
- Balancing System – The balancing system uses two 25 kg scales along with the measured pump speeds to balance the fluid level of the patient. The system will alarm if there is a 50 g discrepancy, or a 20g discrepancy when in "low flow" mode. The actual fluid loss of the patient is measured every second, and the substitution and filtration pumps are sped up or slowed down if the actual fluid loss is higher or lower than the expected fluid loss (page 16.37).
- Heater – The Aquarius system contains a plate heater that heats substitution and/or dialysate solution. The heater can be programmed to heat the solutions from 34 to 39 °C, and can heat up to 6L /hour. The Aquarius system monitors the heater and alarms if the fluid reaches 41 °C or the plate heater reaches 53 °C.
- Air Detector / Blood Saline Detector – The air detector is an ultrasonic detector designed to detect the presence of air in the return blood line. The air detector will trigger an alarm if a 20 μL air bubble is detected at a blood flow rate of 200 ml/min, or 20 μL of "foam" is detected in a 1 minute interval. The housing for the air detector also has an infrared LED used to detect if the tubing is seated correctly, and if blood is present in the tubing. This feature is only used to initiate treatment.
- Return Line Clamp – The return line clamp is located immediately before the return to the patient access, and prevents blood from being re-infused to the patient during some alarm conditions (e.g., air in the tubing).
- Software / Graphical User Interface (GUI) – The Aquarius System, like most modern hemodialysis delivery systems, is a software controlled system with a GUI. The user interacts with the system software using a pressable scroll wheel and series of other buttons on the face of the machine. The GUI is pretend on a 10.4" thin film transistor (TFT) full color monitor. The system also has a red, yellow, and green LED at its top to signal the therapy status to the health care provider.
- Blood Tubing – Edwards has specifically noted that the blood tubing for this system is not included in this 510(k) submission. The blood tubing for this device was cleared under K063293, and was cleared on March 23, 2007.

In case of fault conditions, the system has an audible and visual alarm. The audible alarm is 65 dB at 1 meter, and can be muted for up to 2 minutes. However, if a second alarm occurs while muted, that alarm will sound.

COMPARISON TO PREDICATE

As previously noted, the Aquarius system is virtually identical to the Baxter Accura System (K021615). The firm has also compared their device to the Gambro Prisma System (K993064, K981681, and K946279), and the B.Braun Diapact System (K973322). The primary differences between the Aquarius and the Accura are the addition of the low blood flow feature, the addition of the automatic degassing unit, updated software, and a turnable hook system on the scales for easier loading of solutions. A comparison between the Aquarius and the Accura can be seen in Table 1 below.

Table 1: Comparison between the proposed and predicate devices

	Edwards Aquarius	Baxter Accura
510(k) number	This Submission	K021615
Available treatment modalities	SCUF, CVVH, CVVHD, CVVHDF, TPE	SCUF, CVVH, CVVHD, CVVHDF, TPE
Air detection sensitivity	~ 20 µL	~ 20 µL
Blood leak detections sensitivity	> 0.2 mL blood/min @ 32% Hct	> 0.2 mL blood/min @ 32% Hct
Blood flow rate range (ml/min)	30 – 450 or 10 – 200 (low flow)	30 – 450
Blood flow accuracy	± 10%	± 10%
Scales	Strain gauge capacity ≤ 20 kg ± 0.25%	Strain gauge capacity ≤ 20 kg ± 0.25%
Anticoagulant syringe size (ml)	30 or 50	30 or 50
Heparin delivery	0; 1 to 15 ml/h continuous or 0.5 to 2.5ml bolus	0; 1 to 15 ml/h continuous or 0.5 to 2.5ml bolus
Fluid pumps	Pre-dilution/dialysate, Post-dilution, Effluent	Pre-dilution/dialysate, Post-dilution, Effluent
Pre-Dilution (Dialysate) Pump flow rate*	0: 100 to 10,000 ml/hr for regular 0: 10 to 4,000 ml/hr for low flow	0: 100-10,000 ml/hr
Post-Dilution Pump flow rate*	0: 100 to 10,000 ml/hr for regular 0: 10 to 4,000 ml/hr for low flow	0: 100-10,000 ml/hr
Replacement methods	Pre-dilution Post-dilution Pre+Post (CVVH only)	Pre-dilution Post-dilution Pre+Post (CVVH only)
Effluent pump flow rate (ml/hr)	0: 100-12,000 for regular 0: 10-11,000 for low-flow	0: 100-12000
Access pressure measuring range	-250 to +200 mmHg	-250 to +200 mmHg
Access pressure max alarm limits	-250 to +100 mmHg	-250 to +100 mmHg
Access pressure accuracy	± 5mm Hg	± 5mm Hg
Return pressure measuring range	-50 to +350 mmHg	-50 to +350 mmHg
Return pressure max alarm limits	+10 to +300 mmHg	+10 to +300 mmHg
Return pressure accuracy	± 5mm Hg	± 5mm Hg
Prefilter pressure measuring range	-150 to +500 mmHg	-150 to +500 mmHg
Prefilter pressure max alarm limits	-100 to +500 mmHg	-100 to +500 mmHg
Prefilter pressure accuracy	± 5mm Hg	± 5mm Hg
Effluent pressure measuring range	-250 to +400 mmHg	-450 to +400 mmHg
Effluent pressure max alarm limits	-200 to +350 mmHg for renal -200 to +350 mmHg for TPE	-400 to +400 mmHg for renal -400 to +100 mmHg for TPE
Effluent pressure accuracy	± 10mm Hg	± 10mm Hg
Dialysate / Replacement Heater	Off, 35 °C to 39 °C ± 0.3 °C	Off, 35 °C to 39 °C ± 0.3 °C
*Pre-dilution flow rate + post-dilution flow rate must be < 10,000 mL/hr		

Within their comparison to the predicate devices (Section 12 of the submission), the firm has provided adequate justification for any new or updated features. As such, as long as the proposed device is adequately tested, it can be considered substantially equivalent (SE) to the predicate devices identified.

PERFORMANCE TESTING

Verification and Validation (V&V) information, for both software and hardware, was provided in Section 16.9 of the firm's original submission. This V&V includes component level testing of the primary components of the device, including: blood pump, pre-dilution pump, post-dilution pump, filtration pump, return pressure transducer, access pressure transducer, pre-filter pressure transducer, filtrate pressure transducer, heater, filtrate / substitution scale, air detector, venous clamp, blood leak detector, heparin pump, battery, automatic degassing unit, and power supply. System level testing, including alarm verification, has also been provided. For these tests, Edwards provided the test identification number, a summary of the testing procedure, the expected results, and whether or not the device passed the testing. Additional testing on software specific faults, e.g. faults related to the microprocessor, RAM, or EEPROM chips, was also provided. The firm indicated that the proposed device passed all of the listed testing.

The firm addressed the risks identified in their hazard analysis, and provided traceability to the testing plan provided in Section 16.9 of the original submission. The risks identified by the firm are appropriate for this type of hemodialysis delivery system (e.g., CRRT). In the April 17, 2007, email to the firm, they were asked to provide the complete testing protocols and test results for any mock treatments. The firm has provided this information in Attachment 5 of this submission. Review of the testing protocols confirms that **the performance (bench) testing conducted on the proposed device is adequate to support a substantial equivalence determination.**

Electrical and EMC

In Section 17 of their original submission, Edwards provided conformity to IEC 60601-1 for electrical safety and IEC 60601-1-2 for electromagnetic compatibility (EMC). The device passed this testing. **The electrical and EMC testing for the proposed device can be considered acceptable.**

SOFTWARE

Edwards has submitted software documentation in Section 16 of their original submission. In general, the firm has followed the recommendations of the FDA guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices - Guidance for Industry and FDA Staff." Each of the elements from the guidance document is discussed below.

Level of Concern

In Section 16.1 of their original submission, the firm has correctly identified the proposed software as a "Major" level of concern. Given that the proposed device could cause serious injury or death, **I concur that the software should be considered a "Major" level of concern.**

Software Description

Edwards has provided a basic description of the software in Section 16.1 of their original submission. This information is supplemented by the rest of the submission, including general device description, predicate comparison, and device labeling. Like most hemodialysis delivery systems, and compliant with IEC 60601-2-16, the Aquarius software uses independent software programs and processors to control and monitor the device. The proposed software also contains a third independent program for the display. The names assigned for these software programs are "Master", "Controller", and "Display", respectively.

The functions of the Master software are to control all components of the device and keyboard inquiries as well as to generate and display data. The Master software also controls the main program flow, steers all measuring and regulating units, and is responsible for independently monitoring the Controller software. The Controller software independently monitors many of the measurement results, and compares the values obtained to those being used by the Master software. The Controller software is also responsible for triggering all alarm conditions. The Display software is used to obtain information from the Master software and display it to the user in the form of a graphical user interface (GUI). The GUI of the Aquarius system is virtually identical to that of the Baxter Acura System, and contains on-screen prompts for device setup, programming, general use, troubleshooting, and therapy termination.

The Master and Controller programs were written using "C", and the Display software was written using Pascal. Identification of the specific hardware / microprocessors that the software runs on has been provided in Section 16.2.2 of the original submission.

Software Hazard Analysis

The firm has conducted a hazard analysis using the FDA accepted ISO 14971 methodology. Two separate analyses were conducted; the first includes a listing of risks, potential causes, probability, and severity before mitigation, and the second includes a listing of the mitigation techniques as well as the residual risk levels. The risk analyses conducted by the firm included both hardware and software based failures, and includes all of the relevant risks for hemodialysis delivery systems (e.g., improper therapy, blood loss, air infusion, etc.). **The risk analyses conducted by the firm can be considered acceptable for their intended purpose.**

Software Requirements Specifications (SRS)

Edwards has provided the SRS information in Section 16.4 of their original submission. Each requirement is specifically defined, and adequate information has been provided regarding algorithms used and program logic / flow. The SRS provided by the firm are somewhat high level for device of major level of concern, but **can be considered acceptable for their intended use.**

Architecture Design Charts

Edwards has provided information regarding the system architecture in Section 16.5 of their original submission. This information is provided primarily in graphical format, but contains adequate information to interpret the logic of the software. As previously noted, the software is sub-divided into three separate programs, each running on an independent microprocessor. The "Master" program is responsible for the primary operation of the device, while the "Controller" program is responsible for monitoring the Master program and taking protective action in the

case of an alarm situation. Block diagrams of the functions controlled by the Master and Controller have been provided on pages 16.209 through 16.211 of the original submission. The "Display" program communicates with the Master system to provide the user the graphical user interface (GUI), and translates physical key presses from the user back to the Master software. The three software programs communicate using the RS232 serial interface. **The firm has provided adequate information regarding the architecture of the proposed software.**

Software Design Specifications (SDS)

Edwards has provided their SDS information in Section 16.6 of their original submission. This information includes a "Software Implementation Plan" (16.6.1), a "Software Module Nomenclature" (16.6.2), and a "Software Requirements Implementation" (16.6.3). The first document identifies the name and primary function of each software module in the 3 programs. The second document identifies the naming conventions used during the creation of the software. Finally, the third document provides traceability between the SRS and the specific modules of the software that implement each requirement. **The firm has provided adequate documentation regarding the SDS.**

Traceability Analysis

The firm has included a traceability analysis in Section 16.7 of their original submission. Separate analyses have been provided for the functional requirements specification (e.g., the system as a whole) and the SRS. Each of these analyses link the specific requirements to the verification or validation process used to demonstrate that the requirements are met. The firm also provided an analysis linking the risk analysis to the verification and validation activities. Ideally, a single traceability analysis would have been provided; however, **the information provided by the firm is thorough, and can be considered acceptable for its intended use.**

Development Plan

The firm has provided information regarding their hardware and software development plan in Section 16.8 of their original submission. This information included a definition of the general phases of the Aquarius project, and depictions of the cyclical development model used for the system software. The firm also provided an annotated list of control documents generated during the development process, as well as a copy of the coding standards used to create the software. **The information regarding the development plan of the proposed device provided by the firm can be considered acceptable.**

Verification, Validation, and Testing

All software VV&T provided for the proposed software was provided as system level testing, and is discussed in the "Performance Testing" section above.

Revision Level History

The firm has provided a revision level history starting at version 2.0 (the last common software version with the Baxter Accura) is Section 16.10 of their original submission. Included in this history is each software release version, including specific versions numbers for the master, control, and display software. A basic description of the changes made for each version has also been included in this section. Upon request, the firm has clarified that the release date for this version of the software was January 26, 2007. **Edwards has adequate information regarding the revision level history for this software.**

Unresolved Anomalies (bugs)

Edwards has identified five unresolved anomalies in the current version of software (Section 16.11 of the original submission). They included a description of each anomaly, as well as a rationale regarding why they do not believe the anomaly affect the safety of the device. One issue identified as an anomaly, UA-005, involves balance alarms being generated if one of the fluid lines is clamped. If the line remains clamped, the balance alarm will repeat, which can eventually lead to excessive ultrafiltration form the patient. While this issue can be considered a safety concern, it is more of a training / human factors issue, and not technically a software anomaly. The other bugs listed by the firm should not have an affect on the safety of efficacy of the device. **Therefore, the information provided by the firm can be considered acceptable.**

STERILITY, PACKAGING & BIOCOMPATIBILITY

The only patient contacting portion of this device / system is the Edwards Aqualine Sterile Tubing Sets, which has been submitted under a separate 510(k) currently under review (K063293). As such, **there are no issues regarding sterility, biocompatibility, shelf life, or packaging with this 510(k) submission**.

DEVICE LABELING

Edwards has provides a copy of the draft labeling for the Aquarius System in Section 13 of their original submission. They have also included information regarding the screen layout and a matrix of the messages that will be on the GUI during given situations. The User's manual for the Aquarius System is through, and contains the following sections:

1. How to Use this Manual
2. Getting Started with Aquarius
3. Introducing Aquarius
4. Performing a Treatment with Aquarius
5. Aquarius Alarms and Messages
6. Aquarius Technical Data
7. Guidance and Manufacturer Declaration – Electromagnetic Emissions
8. Aquarius Cleaning and Disinfection
9. Aquarius Warranty and Liability
10. References
11. Index

The User's Manual for the Aquarius System is virtually identical to the manual for the Baxter Accura System (K021615). The manual adequately shows how to setup, prime, program, operate, and troubleshoot the system. It should be noted that much of the setup and troubleshooting information is also contained in the system GUI, and will available to the user when they press the "help" button. Baxter has included adequate warnings regarding fluid composition, including a warning stating that any fluid used as a replacement fluid must be indicated for intravenous (IV) injection (page 13.18). They have also included adequate warnings regarding kinked tubing (page 13.62). In the previous review, several minor labeling deficiencies were identified (see below). **Edwards has addressed these deficiencies, so the proposed labeling can now be considered acceptable.**

ADMINISTRATIVE 510(K) INFORMATION

The firm has included a 510(k) summary, a truthful and accurate statement, and an indications for use statement on a separate page. **This information is acceptable.**

PREVIOUS DEFICIENCIES

The following deficiencies were noted during the course of this review. The firm was notified of the following deficiencies (*italic* font) in an email to their primary contact on April 17, 2007. A summary of the firm's response follows each deficiency.

1. *Please provide additional details regarding the software algorithm used to monitor patient fluid balance. These details should include information regarding how the "Master" and "Controller" software interact with the system scales and fluid pumps to balance fluid, as well as monitoring and controlling system alarm limits. In addition, please provide additional information regarding the potential affect of cumulative fluid balance alarms and how your proposed device mitigates risk to the patient.*

Edwards has provided additional information regarding their fluid balance algorithms in Attachment 1 of this submission. The Master and Controller software programs monitor the system scales and compare the actual change in weight (and therefore fluid) to the prescribed change in weight. The software then uses straightforward linear relationships to scale the pump speeds up or down to maintain appropriate fluid balance. The system is designed to alarm when the fluid discrepancy reaches 50mL (g), or 20mL when using "low flow." In their submission, the firm has acknowledged that if the fluid balance alarms are not adequately resolved, the patient could be at risk due to excessive ultrafiltration, similar to the issue causing the recall of the Gambro Prisma System. Edwards has attempted to mitigate this risk using the graphical user interface of the system, and system labeling. On page 80 of 99 of their User's Manual, they have a warning that states:

> "If repeated balance alarms occur, stop treatment to protect the patient from excessive fluid removal or overload. Call technical support to resolve the problem. Do not use the machine until it has been repaired. If the issue cannot be immediately resolved, end the treatment and remove Aquarius from use until the device is properly calibrated by an Edwards Lifesciences certified technician."

Edwards has provided the information that was requested. Unfortunately, like many CRRT devices on the market, the Aquarius system may be prone to excessive filtration due to user error, which can ultimately result in serious injury or death to the patient. The firm will need to ensure that the users of the Aquarius are well trained regarding the use of the device, with particular attention to fluid balance issues.

2. *Please address the following concerns regarding the User's Manual for your proposed device, and provide updated labeling for FDA review:*

    a. *The indications for use in the user's manual (page 13.8) should match the indications for use you provided for Attachment 4.*

The firm revised the indications for use in the user's manual to match to proposed indications for use. **Edwards has adequately addressed this deficiency.**

b. *The statement "Important: The Anticoagulant pump is designed for heparin only" should be moved from a contraindication to a warning.*

Edwards has moved this statement from a contraindication to a warning.

c. *You have identified several issues and "Exceptions" to labeling requirements in the document entitled "Operators Manual Validation – Final Report" (staring on page 16.689). Please address these issues.*

d. *There are several typographical and grammatical errors in the labeling, presumably due to translational issues. Please address these issues.*

The firm has corrected the "Exceptions" to the labeling and has edited the manual for content, clarity, and grammar. **The labeling for the proposed device can now be considered acceptable.**

3. *Please identify the release date for software version 6.00.04.*

The firm has clarified that the release date for this version of the software was January 26, 2007. **Edwards has adequately addressed this deficiency.**

4. *On page 13.20 of your submission, you have provided users instructions on how to set the date and time of the system software of the proposed device. In light of the recent energy bill passed by Congress in August 2005 that included extending Daylight Saving Time (DST) by about a month, DST would start the second Sunday of March and end on the first Sunday of November. Please indicate if the software of the proposed device has been updated to automatically change for DST, since prior DST had been the first Sunday in April to the last Sunday in October. If not, please perform a hazard analysis in order to determine whether this issue may have an impact on the safety or efficacy of the proposed device. Finally, if you believe the safety or efficacy of the proposed device may be compromised due to this issue, please clarify how you intend to mitigate this risk.*

The firm has clarified that no DST adjustments (either using the old or new DST schedule) is implemented in the software in order to minimize risk. This strategy is acceptable; therefore, **Edwards has adequately addressed this deficiency.**

5. *For all simulated device runs contained in your verification and validation activities (e.g., device testing designed to mimic clinical conditions and run over several hours), please provide the complete testing protocols and the results from this testing.*

The firm has provided this information in Attachment 5 of this submission. Review of the testing protocols confirms that the performance (bench) testing conducted on the proposed device is adequate to support a substantial equivalence determination. **Edwards has adequately addressed this deficiency.**

6. *On page 13.30 of your submission, you recommend changing the hemodialysis filters and blood tubing after 24 hours, but indicate that the tubing has been tested for up to 72 hours. FDA realizes that the blood tubing for your proposed device is not considered part of this 510(k) submission; however, please provide system level testing to indicate that the proposed device can be run safely and effectively over the 24 to 72 hour time period.*

Edwards has provided summaries of their tubing compatibility testing, demonstrating that the Aquarius system can operate with the cleared tubing for up to 75 hours. **Therefore, the firm has adequately addressed this deficiency.**

SUBSTANTIAL EQUIVALENCE DISCUSSION

	Yes	No	
1. Same Indication Statement?	√		If **YES** = Go To 3
2. Do Differences Alter The Effect Or Raise New Issues of Safety Or Effectiveness?			If **YES** = Stop **NSE**
3. Same Technological Characteristics?	√		If **YES** = Go To 5
4. Could The New Characteristics Affect Safety Or Effectiveness?			If **YES** = Go To 6
5. Descriptive Characteristics Precise Enough?		√	If **NO** = Go To 8
			If **YES** = Stop **SE**
6. New Types Of Safety Or Effectiveness Questions?			If **YES** = Stop **NSE**
7. Accepted Scientific Methods Exist?			If **NO** = Stop **NSE**
8. Performance Data Available?	√		If **NO** = Request Data
9. Data Demonstrate Equivalence?	√		Final Decision: **SE**

Note: See http://eroom.fda.gov/eRoomReq/Files/CDRH3/CDRHPremarketNotification510kProgram/0_4148/FLOWCHART%20DECISION%20TREE%20.DOC for Flowchart to assist in decision-making process. Please complete the following table and answer the corresponding questions. "Yes" responses to questions 2, 4, 6, and 9, and every "no" response requires an explanation.

1. Explain how the new indication differs from the predicate device's indication:

N/A, indications for use are the same.

2. Explain why there is or is not a new effect or safety or effectiveness issue:

3. Describe the new technological characteristics:

N/A, technological characteristics use are the same.

4. Explain how new characteristics could or could not affect safety or effectiveness:

5. Explain how descriptive characteristics are not precise enough:

Performance testing is needed to ensure that the proposed device can safely and effectively perform renal replacement therapy.

6. Explain new types of safety or effectiveness question(s) raised or why the question(s) are not new:

7. Explain why existing scientific methods can not be used:

8. Explain what performance data is needed:

The performance testing that is needed for this type of device is outlined in the FDA guidance document for hemodialysis delivery systems (referenced above).

9. Explain how the performance data demonstrates that the device is or is not substantially equivalent:

The performance testing provided by the firm demonstrates that the proposed device operates within its labeled specifications and alarms accordingly under fault conditions. The testing provided by the firm supports a SE determination.

RECOMMENDATION

I recommend that the proposed device be considered substantially (**SE**) equivalent to the predicate devices identified according to 21 CFR 876.5860.

Joshua C. Nipper, M.E. 6/6/07
Date

	YES	NO
Is the device life-supporting or life sustaining?	✓	
Is the device implanted (short-term or long-term)?		✓
Does the device design use software?	✓	
Is the device sterile?		✓
Is the device for single use?		✓
Is the device for over the counter (OTC) use?		✓
Is the device for prescription use?	✓	
Does the device contain a drug or biological product as a component?		✓
Is this device a kit?		✓

C. Neuland 6/6/07

C Neuland 6/6/07 Due to the potential for fluid imbalance problems with CRRT machines if the user is not properly trained, I recommend that a working group be established within FDA to look further into types of additional safeguards which can be put into place to make these types of machines safer.

K070320

Internal Administrative Form

	YES
1. Did the firm request expedited review?	
2. Did we grant expedited review?	✓
3. Have you verified that the Document is labeled Class III for GMP purposes?	NA
4. If, not, has POS been notified?	
5. Is the product a device?	✓
6. Is the device exempt from 510(k) by regulation or policy?	✓
7. Is the device subject to review by CDRH?	
8. Are you aware that this device has been the subject of a previous NSE decision?	
9. If yes, does this new 510(k) address the NSE issue(s), (e.g., performance data)?	NA
10. Are you aware of the submitter being the subject of an integrity investigation?	NO
11. If, yes, consult the ODE Integrity Officer.	
12. Has the ODE Integrity Officer given permission to proceed with the review? (Blue Book Memo #I91-2 and Federal Register 90N0332, September 10, 1991.	NA